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BEFORE THE BOARD OF APPEALS AND INTERFERENCES
OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Goodman et al.	Group Art Unit: 1647
Serial No. 08/971,172	Examiner: Turner, S.
Filed: November 14, 1997	Attorney Docket No.B98-006-2
For: *Robo: A Novel Family of Polypeptides and Nucleic Acids*	CERTIFICATE OF MAILING I hereby certify that this corr. is being deposited with the US Postal Service as First Class Mail in an envelope addressed to the Comm. for Patents, Washington, D.C. 20231 on June 26, 2002. Signed _____ Richard Osman

BRIEF ON APPEAL

The Honorable Board of Appeals and Interferences
United States Patent and Trademark Office
Washington, D.C. 20231

Dear Honorable Board:

This is an appeal from the October 10, 2001 final rejection of claims 68-91 and 93-119.

REAL PARTY IN INTEREST

The real parties in interest are The Regents of the University of California and Renovis, Inc., the Assignee and Licensee, respectively, of this application.

RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any related appeals or interferences.

STATUS OF THE CLAIMS

Claims 68-91 and 93-119 are pending and subject to this appeal.

STATUS OF THE AMENDMENTS

The 6/17/02 Advisory Action indicated our 1/14/02 Amendment correcting punctuation would be entered upon filing an appeal; accordingly, all Amendments are believed to be properly before the Board.

SUMMARY OF THE INVENTION

The claimed invention relates to diagnostic probes that specifically detect Robo proteins or transcripts. Robo proteins comprise a key component of the body's nerve cell guidance system. In particular, the inventors disclose that Robo functions as the critical gatekeeper controlling midline crossing of spinal axons (Specification, p.2, line 28 - p.3, line 2). These neural guidance molecules provide for proper enervation during development, but also prevent regeneration of proper nerve pathways following spinal injuries in adults. Hence, Robo polypeptides are important targets for therapeutic intervention (e.g. Specification, p.13, line 28 - p.14, line 20) and the ability to trace the presence of Robo in spinal tissue (e.g. Specification, p.29, lines 16-17; p.14, line 30 - p.17, line 18; p.20, line 30 - p.21, line 6; p.29, lines 14-16; p.31, lines 30-31; p.34, line 22 - p.35, line 4; etc.) is critical to developing therapy for spinal injuries.

ISSUES

I. WHETHER CLAIMS 68-91 AND 93-119 ARE PATENTABLE UNDER 35USC101

II. WHETHER CLAIMS 68-91 AND 93-119 ARE PATENTABLE UNDER 35USC112, FIRST PARAGRAPH

III. WHETHER CLAIMS 81, 100, 102-104 AND113-114 ARE PATENTABLE UNDER 35USC112, FIRST PARAGRAPH

IV. WHETHER CLAIMS 88-90 ARE PATENTABLE UNDER 35USC102(a)

V. WHETHER CLAIMS 108-110 ARE PATENTABLE UNDER 35USC102(a)

VI. WHETHER CLAIMS 94-95 ARE PATENTABLE UNDER 35USC103(a)

GROUPING OF THE CLAIMS

For issue I, claims 68-71, 73-74; 79-81, 83-84, 88-91, 94-95, 100-104, 106-107, 112-114, 116-117 shall stand as a separate group; and claims 72, 78, 82, 87, 93, 99, 105, 111, 115 shall stand as a separate group.

For issue II, claims 68-71, 73-74; 79-81, 83-84, 88-91, 94-95, 100-104, 106-107, 112-114, 116-117 shall stand as a separate group; and claims 72, 78, 82, 87, 93, 99, 105, 111, 115 shall stand as a separate group.

For Issue III, claim 81 shall stand separately; claims 100, 102-103 shall stand as a separate group; claim 104 shall stand separately; claim 113 shall stand separately; and claim 114 shall stand separately.

For Issue IV, the rejected claims shall stand as a group.

For Issue V, the rejected claims shall stand as a group.

For Issue VI, the rejected claims shall stand as a group.

ARGUMENT

I. CLAIMS 68-91 AND 93-119 ARE PATENTABLE UNDER 35USC101

Claim 68-91 AND 93-119 relate to diagnostic probes that specifically detect Robo proteins or transcripts. Robo proteins comprise a key component of the body's nerve cell guidance system. In particular, the inventors disclose that Robo functions as the critical gatekeeper controlling midline crossing of spinal axons (Specification, p.2, line 28 - p.3, line 2). These neural guidance molecules provide for proper enervation during development, but also prevent regeneration of proper nerve pathways following spinal injuries in adults. Hence, Robo polypeptides are important targets for therapeutic intervention (e.g. Specification, p.13, line 28 - p.14, line 20) and the ability to trace the presence of Robo in spinal tissue (e.g. p.29, lines 16-17; p.14, line 30 - p.17, line 18; p.20, line 30 - p.21, line 6; p.29, lines 14-16; p.31, lines 30-31; p.34, line 22 - p.35, line 4; etc.) is critical to developing therapy for spinal injuries.

The claims are limited to particularly useful diagnostic probes. The polynucleotides of claims 68, 79, 88, 100 and 112 (and their dependencies) encode polypeptides which elicit a corresponding Robo-specific antibody probe. As taught by our Specification (supra), these probes are useful to trace

the presence of Robo expression in tissue. The polynucleotides of claims 75, 85, 96, 108 and 118 (and their dependencies) provide specific hybridization probes for the corresponding Robo-1 mRNA. As taught by our Specification (supra), these probes are useful to trace the presence of Robo expression in tissue.

The Action misconstrues the claims to require that the reagents serve to diagnose or treat disease. No such requirement is present in the claims. As repeatedly used in the specification, the probes are diagnostic of the presence of Robo transcripts and protein; e.g. p.3, lines 12-13. These probes are as industrially useful as any equipment or reagents used in commercial research. For example, specific antibodies diagnostic of the presence of nerve guidance molecules are commercially bought, sold and licensed. Product data sheets from Santa Cruz Biotechnology, Inc., and the Development Studies Hybridoma Bank (made of record with our Response mailed January 14, 2002) document present, real-world, industrial commerce (buying and selling) of probes for natural nerve guidance molecules, including three different anti-Robo antibody reagents. Unlike the invention in Brenner v. Manson, here the record documents a present, real-world commercial market for the invention.

The polynucleotides of claims 68-71, 73-74; 79-81, 83-84; 88-91, 94-95; 100-104, 106-107; 112-114, 116-117 are required to encode polypeptides which elicit a corresponding Robo-specific antibody. As noted above, Robo-specific antibodies are articles of present, real-world, industrial commerce (buying and selling). As these claims are specifically limited to reagents used in the manufacture of present, real-world, industrial commercial products, they are even further removed from the pending 35USC101 rejection.

The polynucleotides of claims 72, 82, 93, 105 and 115, are required to encode a full-length Robo protein. Similarly, claims 78, 87, 99, 111 each require a full-length Robo cDNA, so these polynucleotides also necessarily encode a full-length Robo protein. Not only are these reagents used in the manufacture of present, real-world, industrial commercial products (e.g. Robo-specific antibodies), they encode natural, fully functional Robo proteins which have been demonstrated to regulate neural guidance and provide important targets for therapeutic intervention. Hence, these claims are even further removed from the pending 35USC101 rejection.

II. CLAIMS 68-91 AND 93-119 ARE PATENTABLE UNDER 35USC112, FIRST PARAGRAPH

Claims 68-91 and 93-119 are supported by a specific and substantial, credible asserted utility, (supra), and hence, one skilled in the art would clearly know how to use the claimed invention. In fact, use of Robo-specific probes as claimed is expressly described, e.g. p.29, lines 14-16 and 16-17. The invention defines commercially useful subject matter (supra) and the Specification shows one skilled in the art knows how to use the claimed invention (supra).

The polynucleotides of claims 68-71, 73-74; 79-81, 83-84; 88-91, 94-95; 100-104, 106-107; 112-114, 116-117 are required to encode polypeptides which elicit a corresponding Robo-specific antibody. As noted above, Robo-specific antibodies are articles of present, real-world, industrial commerce (buying and selling). As these claims are specifically limited to reagents used in the manufacture of present, real-world, industrial commercial products, they are even further removed from this 35USC112, first paragraph rejection.

The polynucleotides of claims 72, 82, 93, 105 and 115, are required to encode a full-length Robo protein. Similarly, claims 78, 87, 99, 111 each require a full-length Robo cDNA, so these polynucleotides also necessarily encode a full-length Robo protein. Not only are these reagents used in the manufacture of present, real-world, industrial commercial products (e.g. Robo-specific antibodies), they encode natural, fully functional Robo proteins which have been demonstrated to regulate neural guidance and provide important targets for therapeutic intervention. Hence, these claims are even further removed from this 35USC112, first paragraph rejection.

III. CLAIMS 81, 100, 102-104 AND 113-114 ARE PATENTABLE UNDER 35USC112, FIRST PARAGRAPH

Claims 81, 100, 102-104, 113-114 are supported by a proper written description; in particular:

Claim 81: The polypeptide defined by residues 1-942 of SEQ ID NO:4 was separately disclosed in Table 1 as filed. That we provided an alignment of this polypeptide with other robo family members does not diminish the fact that it is separately disclosed. Furthermore, the Specification teaches that the polypeptides of the invention include incomplete translates and deletion mutants of SEQ

ID NO:4 (p.4, lines 6-8). In fact, this particularly disclosed polypeptide defines a robo domain (extracelluar domain) taught to be advantageously specifically targeted with monoclonal antibodies (p.29, lines 16-17).

Claims 100, 102-104: The polypeptide defined by residues 68-259 of SEQ ID NO:8 was separately disclosed on p.4, line 19 of the Specification as filed. The recitation in claim 104 is identical to that on p.4, line 19. The cited sequence (68-259) does not appear in claims 100 and 102-103, so these claims are grouped separately.

Claims 113-114: The polypeptide defined by residues 1-284 of SEQ ID NO:10 was separately disclosed in Table 1 as filed. That we provided an alignment of this polypeptide with other robo family members does not diminish the fact that is separately disclosed. Furthermore, the Specification teaches that the polypeptides of the invention include incomplete translates and deletion mutants of SEQ ID NO:10 (p.4, lines 6-8). The cited sequence (1-284) does not appear in claim 113 so this claim is grouped separately.

IV. CLAIMS 88-90 ARE PATENTABLE UNDER 35USC102(a)

Claims 88-90 are free of the cited art. The Sptrembl-11 seq. O01632 was made of record by the present Examiner in her Action mailed 1/21/00; on the accompanying PTO-892 she indicated for this sequence a date of 7/1/97, and the accompanying sequence printout indicated a record creation date of 7/1/97, and a last annotation update date of 11/1/98. In addition, someone from the PTO handwrote on the record printout next to the 7/1/98 creation date, "Public availability date".

As we have previously explained, O01632 is identical in sequence to EMBL/GenBank amino acid entry 1825710, which was generated and submitted by the same authors, but was reportedly released earlier, on Apr 21, 1997. 1825710 (and O01632) appear to encode residues 424-1297 of our SEQ ID NO:6.

Also on Apr 21, 1997, Genbank reportedly released U88183 and 1825711. U88183 (which we made of record in our Response transmitted on 2/7/00) is the sequence of X chromosome cosmid ZK377 and its annotation includes predicted open reading frames, including 1825710 and 1825711. 1825711 appears to encode residues 1-423 of SEQ ID NO:6. Hence, the sequence of natural C. elegans robo (SEQ ID NO:6, also known as sax-3, see p.28, line 2 of our specification) comprises a

recombination of 1825710 and 1825711. Note that the annotation reference to the Wilson (1994) reference describing a chromosome III cosmid is not for any X chromosome sequence, but merely for methods used to sequence large parts of C. elegans chromosomes.

To the extent that the sequences of the 1825710 and 1825711 predicted reading frames are citeable art under 35USC102(a), our Supplemental Declaration under 37CFR1.131 (made of record with our Response mailed Aug 31, 2000) demonstrates that Applicants had possession of the claimed subject matter prior to their publication. Specifically, the Declaration shows that the full-length sequence encoding C. elegans robo (SEQ ID NO:6) was determined by Applicants prior to the April 21, 1997 publication dates of 1825710 and 1825711.

The appealed-from Action makes numerous inaccurate representations and appends what appears to be a printout of an electronic record relating to U88183. First, we did not make any of the admissions alleged by the Examiner and have respectfully requested that if she wishes to rely on our statements in the record, she quote them accurately and completely. Second, the creation date of an EMBL or GenBank record is not the public availability date. The creation date is the date the record was originally created. Frequently, these records are maintained in secrecy until a predetermined publication or patent filing date is effected. Furthermore, the record at the creation date does not often reflect the record as subsequently accessed. Like most electronic databases, Genbank and EMBL are constantly updating, amending, annotating and otherwise supplementing their records. These newer "editions" retain the creation date of the original record, but were obviously not in existence at that date. Here, the Examiner seeks to rely on a creation date for a record that could not logically have existed on that creation date. A document (electronic or otherwise) that makes explicit reference to dates and events in Apr 1997 and Mar 2000 could not logically have been "published" or made "publically available" in Feb 1997. This rejection is akin to citing a year 2002-updated article in the Encyclopedia Brittanica and relying on the encyclopedia's year 1768 original publication date.

Highlighted copies of EMBL and GenBank database information for submitters (including information on withholding public availability of records after submission and record creation) were made of record with our Response mailed January 14, 2002. Also made of record with our Response mailed January 14, 2002 was a Sample GenBank Record explaining that even the date of last modification may not correspond to the release date (see highlighted, sixth page of Sample GenBank

Record).

V. CLAIMS 108-110 ARE PATENTABLE UNDER 35USC102(a)

Claims 108-110 are free of the cited art. As noted in our Second Declaration under 37CFR1.131 (filed with our Response mailed 8/31/00) the Word document appended thereto describes a cDNA sequence including the 5' UTR of Human Robo1 (bases 1-509) and Human Robo1 coding sequence (bases 510-5366) encoding amino acids 1-1619 of Human Robo 1. Claims 108-110 are limited to polynucleotide sequences within this cDNA; hence, Applicants have documented possession of the invention as claimed prior to the purported publication date of the GenBank Accession No. Z95705.

More particularly, claims 108-110 encompass polynucleotides comprising a sequence falling within the bounds of SEQ ID NO:7, nucleotides 134-3630. This sequence is identical to the sequence bound by nucleotides 643-4139 as shown in the cited Word document; in fact, nucleotides 1-4856 of SEQ ID NO:7 are identical to nucleotides 510-5365 as shown in the cited Word document. A marked up copy of the Word document, showing the boundaries corresponding to SEQ ID NO:7, nucleotides 1-4859 and 134-3630 was made of record with our Response mailed January 14, 2002.

VI. CLAIMS 94-95 ARE PATENTABLE UNDER 35USC103(a)

Claims 94-95 are free of the cited art because the GenBank Accession No. O01632 (U88183) upon which the Action principally relies is not prior art for the reasons explained above.

Appellants respectfully request reversal of the pending Final Action by the Board of Appeals.

We petition for and authorize charging our Deposit Account No.19-0750 all necessary extensions of time. The Commissioner is authorized to charge any fees or credit any overcharges relating to this communication to our Dep. Acct. No.19-0750 (order B98-006-2.)

Respectfully submitted,
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CLAIMS ON APPEAL

68. An isolated polynucleotide comprising a coding strand encoding a polypeptide comprising a sequence of at least 12 consecutive residues of SEQ ID NO:2, wherein the polypeptide elicits a Drosophila Robo-1 (SEQ ID NO:2) specific antibody.

69. An isolated polynucleotide according to claim 68, wherein the sequence comprises at least 32 consecutive residues of SEQ ID NO:2 .

70. An isolated polynucleotide according to claim 68, wherein the sequence comprises at least 64 consecutive residues of SEQ ID NO:2.

71. An isolated polynucleotide according to claim 68, wherein the sequence is selected from the group consisting of residues 30-46, 56-152, 153-251, 252-344, 345-440, 441-535, 536-635, 636-753, 754-854, 915-938, 1037-1046, 1098-1119, 1262-1269 of SEQ ID NO:2.

72. An isolated polynucleotide according to claim 68, wherein the sequence is SEQ ID NO:2.

73. A cell comprising a polynucleotide according to claim 68.

74. A method for making a Robo polypeptide, comprising the steps of: incubating a host cell or cellular extract containing a polynucleotide according to claim 68 under conditions whereby the polypeptide is expressed and recovering the polypeptide.

75. An isolated polynucleotide comprising at least 24 consecutive nucleotides of SEQ ID NO:1, wherein the polynucleotide provides a specific hybridization probe for Drosophila Robo-1 mRNA (RNA equivalent of SEQ ID NO:1).

76. An isolated polynucleotide according to claim 75, comprising at least 36 consecutive nucleotides of SEQ ID NO:1.

77. An isolated polynucleotide according to claim 75, comprising at least 96 consecutive nucleotides of SEQ ID NO:1.

78. An isolated polynucleotide according to claim 75, comprising SEQ ID NO:1.

79. An isolated polynucleotide comprising a coding strand encoding a polypeptide comprising a sequence of at least 12 consecutive residues of SEQ ID NO:4, wherein the polypeptide elicits a Drosophila Robo-2 (SEQ ID NO:4) specific antibody.

80. An isolated polynucleotide according to claim 79, wherein the sequence comprises residues 4-99, 100-192, 193-296, 297-396, 397-494, 495-595, 596-770, 771-877, 906-929, and 1075-1084 of SEQ ID NO:4.

81. An isolated polynucleotide according to claim 79, wherein the sequence comprises residues 1-942 of SEQ ID NO:4.

82. An isolated polynucleotide according to claim 79, wherein the sequence comprises SEQ ID NO:4.

83. A cell comprising a polynucleotide according to claim 79.

84. A method for making a Robo polypeptide, comprising the steps of: incubating a host cell or cellular extract containing a polynucleotide according to claim 79 under conditions whereby the polypeptide is expressed and recovering the polypeptide.

85. An isolated polynucleotide comprising at least 36 consecutive nucleotides of SEQ ID NO:3, wherein the polynucleotide provides a specific hybridization probe for Drosophila Robo-2 mRNA (RNA equivalent of SEQ ID NO:3).

86. An isolated polynucleotide according to claim 85, comprising at least 96 consecutive nucleotides of SEQ ID NO:3.

87. An isolated polynucleotide according to claim 85, comprising SEQ ID NO:3.

88. An isolated polynucleotide comprising a coding strand encoding a polypeptide comprising a sequence of at least 12 consecutive residues of SEQ ID NO:6, wherein the polypeptide elicits a C. Elegans (SEQ ID NO:6) specific antibody.

89. An isolated polynucleotide according to claim 88, wherein the sequence comprises at least 32 consecutive residues of SEQ ID NO: 6.

90. An isolated polynucleotide according to claim 88, wherein the sequence comprises at least 64 consecutive residues of SEQ ID NO: 6.

91. An isolated polynucleotide according to claim 88, wherein the sequence is selected from the group consisting of residues 30-129, 130-223, 224-315, 316-453, 454-543, 544-643, 644-766, 767-865, 900-922, 1036-1045, 1153-1163, and 1065-1074 of SEQ ID NO:6.

93. An isolated polynucleotide according to claim 88, wherein the sequence is SEQ ID NO:6.

94. A cell comprising a polynucleotide according to claim 88.

95. A method for making a Robo polypeptide, comprising the steps of: incubating a host cell or cellular extract containing a polynucleotide according to claim 88 under conditions whereby the polypeptide is expressed and recovering the polypeptide.

96. An isolated polynucleotide comprising at least 24 consecutive nucleotides of SEQ ID NO:5, wherein the polynucleotide provides a specific hybridization probe for C. elegans Robo mRNA (RNA equivalent of SEQ ID NO:5).

97. An isolated polynucleotide according to claim 96, comprising at least 36 consecutive nucleotides of SEQ ID NO:5.

98. An isolated polynucleotide according to claim 96, comprising at least 96 consecutive nucleotides of SEQ ID NO:5.

99. An isolated polynucleotide according to claim 96, comprising SEQ ID NO:5.

100. An isolated polynucleotide comprising a coding strand encoding a polypeptide comprising a sequence selected from the group consisting of residues 1-12, 18-28, 31-40, 45-65, 106-116, 137-145, 214-230, 274-286, 314-324, 399-412, 496-507, 548-565, 599-611, 660-671, 717-730, 780-791, 835-847, 877-891, 930-942, 981-998, 1040-1051, 1080-1090, 1154-1168, 1215-1231, and 1278-1302 of SEQ ID NO:8, or the group consisting of residues 6-21, 68-167, 168-258, 259-350, 351-450, 451-546, 547-644, 645-761, 762-862, 896-917, 1070-1079 and 1181-1195 of SEQ ID NO:8, wherein the polypeptide elicits a human Robo-1 (SEQ ID NO:8) specific antibody.

101. An isolated polynucleotide according to claim 100, wherein the sequence is selected from the group consisting of residues 1-12, 18-28, 31-40, 45-65, 106-116, 137-145, 214-230, 274-286, 314-324, 399-412, 496-507, 548-565, 599-611, 660-671, 717-730, 780-791, 835-847, 877-891,

930-942, 981-998, 1040-1051, 1080-1090, 1154-1168, 1215-1231, and 1278-1302 of SEQ ID NO:8.

102. An isolated polynucleotide according to claim 100, wherein the sequence is selected from the group consisting of residues 6-21, 68-167, 168-258, 259-350, 351-450, 451-546, 547-644, 645-761, 762-862, 896-917, 1070-1079, and 1181-1195 of SEQ ID NO:8.

103. An isolated polynucleotide according to claim 100, wherein the sequence is selected from the group consisting of residues 1-67, 68-167, 168-259, 260-350 and 351-451 of SEQ ID NO:8.

104. An isolated polynucleotide according to claim 100, wherein the sequence is selected from the group consisting of residues 1-167, 68-259, 1-67 joined to 168-259, and 1-67 joined to 260-451 of SEQ ID NO:8.

105. An isolated polynucleotide according to claim 100, wherein the sequence comprises SEQ ID NO:8.

106. A cell comprising a polynucleotide according to claim 100.

107. A method for making a Robo polypeptide, comprising the steps of: incubating a host cell or cellular extract containing a polynucleotide according to claim 100 under conditions whereby the polypeptide is expressed and recovering the polypeptide.

108. An isolated polynucleotide comprising a sequence selected from the group consisting of nucleotides 134-501, 502-776, 777-1049, 1051-1350, 1351-1636, 1637-1933, 1934-2284, 2285-2589, 2666-2765, 3169-3268, and 3514-3613 of SEQ ID NO:7; or the group consisting of nucleotides 199-228, 777-806, 1051-1080, 1352-1381, 1637-1666, 1934-1963, 2285-2313, 2643-

2672, 3172-3200, and 3491-3520 of SEQ ID NO:7; or the group consisting of a reverse complement of a sequence selected from nucleotides 471-500, 751-777, 1021-1050, 1321-1350, 1607-1636, 1902-1931, 2257-2286, 2561-2591, 2761-2790, 3281-3310 and 3601-3630 of SEQ ID NO:7, wherein the polynucleotide provides a specific hybridization probe for human Robo-1 mRNA (RNA equivalent of SEQ ID NO:7).

109. An isolated polynucleotide according to claim 108, wherein the sequence is selected from the group consisting of nucleotides 134-501, 502-776, 777-1049, 1051-1350, 1351-1636, 1637-1933, 1934-2284, 2285-2589, 2666-2765, 3169-3268, and 3514-3613 of SEQ ID NO:7.

110. An isolated polynucleotide according to claim 108, wherein the sequence is selected from the group consisting of nucleotides 199-228, 777-806, 1051-1080, 1352-1381, 1637-1666, 1934-1963, 2285-2313, 2643-2672, 3172-3200, and 3491-3520 of SEQ ID NO:7; or the group consisting of a reverse complement of a sequence selected from nucleotides 471-500, 751-777, 1021-1050, 1321-1350, 1607-1636, 1902-1931, 2257-2286, 2561-2591, 2761-2790, 3281-3310 and 3601-3630 of SEQ ID NO:7.

111. An isolated polynucleotide according to claim 108, comprising SEQ ID NO:7.

112. An isolated polynucleotide comprising a coding strand encoding a polypeptide comprising a sequence selected from the group consisting of residues 5-16, 38-47, 83-94, 112-125, 168-180, 195-209, 222-235, and 241-254 of SEQ ID NO:10, wherein the polypeptide elicits a human Robo-2 (SEQ ID NO:10) specific antibody.

113. An isolated polynucleotide according to claim 112, wherein the sequence is selected from the group consisting of residues 1-91, 92-185, and 186-282 of SEQ ID NO:10.

114. An isolated polynucleotide according to claim 112, wherein the sequence comprises residues 1-284 of SEQ ID NO:10.

115. An isolated polynucleotide according to claim 112, wherein the sequence comprises SEQ ID NO:10.

116. A cell comprising a polynucleotide according to claim 112.

117. A method for making a Robo polypeptide, comprising the steps of: incubating a host cell or cellular extract containing a polynucleotide according to claim 112 under conditions whereby the polypeptide is expressed and recovering the polypeptide.

118. An isolated polynucleotide comprising a sequence selected from the group consisting of nucleotides 7-36, 274-303 and 566-592 of SEQ ID NO:9; or the group consisting of a reverse complement of a sequence selected from nucleotides 244-273, 528-557, 800-826 of SEQ ID NO:9, wherein the polynucleotide provides a specific hybridization probe for human Robo-2 mRNA (RNA equivalent of SEQ ID NO:9).

119. An isolated polynucleotide according to claim 118, wherein the sequence is selected from the group consisting of nucleotides 1-273, 274-558, and 559-854 of SEQ ID NO:9.